Decision Summary

We have fully considered Boston Scientific Corporation's request to reconsider our National Coverage Determination (NCD) on percutaneous transluminal angioplasty (PTA) with intracranial stent placement that is published at 20.7.B.5 of the Medicare National Coverage Determinations Manual. After considering additional evidence and information, including the timely public comments as required by §1862(1) of the Social Security Act, we are reaffirming our existing national coverage decision and will not expand coverage as requested. Medicare will continue to cover PTA and stenting of intracranial arteries for the treatment of cerebral artery stenosis ≥ 50% in patients with intracranial atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE trials. CMS will continue our national non-coverage for all other indications for PTA with or without stenting to treat obstructive lesions of the vertebral and cerebral arteries.

Back to Top

Decision Memo

TO: Administrative File: CAG 00085R5
Decision Memorandum for Intracranial Stenting and Angioplasty

FROM:

Steve Phurrough, MD, MPA
Director, Coverage and Analysis Group

Marcel Salive, MD, MPH
Director, Division of Medical and Surgical Services

Sandy Jones, RN, MS
Lead Analyst

Joseph Chin, MD
Lead Medical Officer

SUBJECT: Decision Memorandum for Intracranial Stenting and Angioplasty

DATE: May 12, 2008

I. Decision

We have fully considered Boston Scientific Corporation's request to reconsider our National Coverage Determination (NCD) on percutaneous transluminal angioplasty (PTA) with intracranial stent placement that is published at 20.7.B.5 of the Medicare National Coverage Determinations Manual. After considering additional evidence and information, including the timely public comments as required by §1862(1) of the Social Security Act, we are reaffirming our existing national coverage decision and will not expand coverage as requested. Medicare will continue to cover PTA and stenting of intracranial arteries for the treatment of cerebral artery stenosis $\geq$ 50% in patients with intracranial atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE trials. CMS will continue our national non-coverage for all other indications for PTA with or without stenting to treat obstructive lesions of the vertebral and cerebral arteries.

II. Background

Intracranial angioplasty and stenting is a relatively novel approach for the treatment of refractory, symptomatic intracranial artery stenosis. CMS previously issued a national coverage determination on intracranial PTA and stenting, §20.7.B.5 of the Medicare National Coverage Determination Manual. Our final decision memorandum, dated November 6, 2006 describes the background, earlier history of coverage and analyzes evidence available up to that time (see: http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=177). We are incorporating the final decision memorandum as part of the record of this decision memorandum.[1]

In August 2007, CMS accepted a formal request from Boston Scientific Corporation to reconsider coverage for intracranial stenting and angioplasty using the Wingspan® Stent System with Gateway™ Percutaneous Transluminal Angioplasty (PTA) Balloon Catheter for the treatment of intracranial arterial stenosis $\geq$ 50%.

III. History of Medicare Coverage

Effective November 6, 2006, the Medicare National Coverage Determination (NCD) Manual (20.7.B.5) for PTA states that stenting of the intracranial arteries has been conditionally covered to treat cerebral artery stenosis as follows.

"Medicare covers PTA and stenting of intracranial arteries for the treatment of cerebral artery stenosis $\geq$ 50% in patients with intracranial atherosclerotic disease when furnished in accordance with the [Food and Drug Administration] FDA- approved protocols governing Category B [Investigational Device Exemption] IDE clinical trials. CMS determines that coverage of intracranial PTA and stenting is reasonable and necessary under these circumstances."[2]

On August 24, 2007, CMS received a formal request for reconsideration of the National Coverage Determination (NCD) for Percutaneous Transluminal Angioplasty (PTA) from the Wingspan® Stent System with Gateway™ PTA Balloon Catheter manufacturer, Boston Scientific Corporation. The manufacturer requests that CMS update its NCD to permit broader coverage including the possible use of coverage with evidence development, for intracranial stenting and angioplasty for patients with intracranial atherosclerotic disease, refractory to medical therapy in intracranial vessels with greater than or equal to 50 percent stenosis.

Benefit Category
Medicare is a defined benefit program. A prerequisite for Medicare coverage is that an item or service must meet one of the statutorily defined benefit categories in the Social Security Act and not otherwise be excluded from coverage. Intracranial stenting and angioplasty at a minimum, falls under the benefit category set forth in §1861(b)(3) (inpatient hospital services), a part A benefit under §1812(a)(1) and §1861(s)(1) (physician services), a part B benefit.

IV. Timeline of Recent Activities

Date	Action
August 24, 2007	CMS accepts Boston Scientific Corporation’s formal NCD reconsideration request for expanded coverage of intracranial stenting and angioplasty. The tracking sheet is posted and the initial 30-day comment period begins.
September 18, 2007	CMS met with Boston Scientific Corporation’s staff to discuss their proposed observational clinical study for consideration under coverage with evidence development.
September 23, 2007	Initial 30 day public comment period closes. Comments are posted on the website.
January 7, 2008	CMS received Boston Scientific Corporation’s revised observational study.
February 14, 2008	CMS posted the proposed decision memorandum.
March 15, 2008	30-day public comment period closes.

Date	Action
May 12, 2008	Final decision memorandum posted and effective. No change to the NCD of November 6, 2006.

V. FDA Status

Congress has designated the FDA responsibility for review and approval of Humanitarian Use Devices (HUDs) that are used to treat or diagnose a disease or condition that affects fewer than 4,000 individuals in the United States. A Humanitarian Device Exemption (HDE) allows the HUD device to be marketed for a specific condition. The device manufacturer must submit an humanitarian device exemption (HDE) application, which is similar in both form and content to a premarket approval (PMA) application, but is exempt from the effectiveness requirements of a PMA. An HDE application is not required to contain the results of scientifically valid clinical investigations demonstrating that the device is effective for its intended purpose. The application, however, must contain sufficient information for FDA to determine that the device does not pose an unreasonable or significant risk of illness or injury and that the probable benefit to health outweighs the risk of injury or illness from its use, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment. Additionally, the applicant must demonstrate that no comparable devices are available to treat or diagnose the disease or condition, and that they could not otherwise bring the device to market.

An approved HDE authorizes marketing of the HUD. However, a HUD may be used only in facilities with properly constituted and functioning Institutional Review Boards (IRBs). IRB approval is required before a HUD is used at a facility, with the exception of certain emergency uses. The HUD applicant must assure the costs of the device do not exceed the costs of research, development, manufacturing and distribution of the device unless the HUD is indicated for use in pediatric patients and has been determined by FDA to be narrowly exempt from the prohibition on profit. Finally, HDE holders must provide FDA with periodic reports demonstrating that the HUD designation is still valid, based on the most current and authoritative information available.[3]

On August 3, 2005, the FDA, Center for Devices and Radiological Health (CDRH), approved Boston Scientific Corporation's HDE application for the Wingspan® Stent System with Gateway™ PTA Balloon Catheter for the treatment of medically refractory ICAD to improve the intracranial vasculature accessible to this device in symptomatic patients with $\geq$ 50% stenosis. The FDA letter[4] refers to this application submitted by Boston Scientific Corporation and the public was notified of this FDA decision.[5] Based on the data submitted with the HDE application, the Gateway™ PTA Balloon Catheter Stent System will not expose patients to an unreasonable or significant risk of illness or injury. Additionally, when the device is used following the instructions for use, it has been determined that there is a probable benefit to health that outweighs the risks of illness or injury, taking into account the probable risks and benefits of currently available devices or alternative forms of treatment.

CMS does not have a national policy that addresses coverage of HUDs. Currently, contractors have the discretion to provide coverage for these devices in the absence of a national coverage determination. A HUD is nationally not covered if it falls under the purview of an NCD which nationally non-covers the device or service for which the HUD may be used.

VI. General Methodological Principles

When making national coverage decisions, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member. The evidence may consist of external technology assessments, internal review of published and unpublished studies, recommendations from the Medicare Coverage Advisory Committee, evidence-based guidelines, professional society position statements, expert opinion and public comments. The critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific clinical questions relevant to the coverage request can be answered conclusively; and 2) the intervention will improve patients' health outcomes. (The General Methodological Principles of Study Design is located in *Appendix A*.)

We, generally, divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

Public comments sometimes cite the published clinical evidence and gives CMS useful information. Public comments that give information on unpublished evidence such as results of individual practitioners or patients are less rigorous and therefore less useful when making a coverage determination. CMS uses the initial public comments to inform its proposed decision. CMS responds in detail to the public comments on a proposed decision when issuing the final decision memorandum.

VII. Evidence

A. Introduction

In this reconsideration, we considered studies and evidence that were published after the prior decision that addressed intracranial angioplasty and stenting in 2006. Health outcomes of interest include mortality, stroke, adverse events and restenosis (development of a new obstructive lesion in the treated segment). Although often reported, the ability to successfully perform the stenting and angioplasty or the ability to increase the intracranial artery lumen diameter are not sufficient outcomes by themselves. These outcomes indicate the feasibility of applying the intervention; however, while a necessary first step, procedural outcomes do not provide evidence on the health outcomes of interest to CMS.

Literature Search

CMS searched PubMed (2006 to present) for publications of randomized clinical trials (RCTs), observational studies and reviews on intracranial stenting and angioplasty. General keywords included intracranial, stenting, angioplasty and Wingspan®. Studies must have presented original data and been published in peer-reviewed English language journals. After an initial scan of the literature that included other intracranial stent systems, our search was narrowed to include only studies that used the Wingspan® system since other stents were not self-expanding and have not been FDA approved for uses in the intracranial arteries. Abstracts and animal studies were excluded.

B. Discussion of evidence reviewed

1. Question

-

- Is the evidence sufficient to conclude that percutaneous transluminal angioplasty and stenting of symptomatic intracranial artery stenosis $\geq$ 50% improves health outcomes?

2. External technology assessments

We did not request an external technology assessment on this issue and are not aware of any other similar assessments.

3. Internal technology assessment

Bose A, Hartmann M, Henkes H, et al. A novel, self-expanding, nitinol stent in medically refractory intracranial atherosclerotic stenoses: the Wingspan study. Stroke 2007;38(5):1531-1537.

Bose and colleagues published the results of a case series of 45 patients "to assess the safety and performance of the Wingspan[®] stent system and Gateway[™] percutaneous transluminal angioplasty balloon catheter in the treatment of high-grade, intracranial atherosclerotic lesions in patients who had failed medical therapy." Inclusion criteria included symptomatic intracranial atherosclerotic stenosis $\geq$ 50% in a vessel 2.5 to 4.5 mm in diameter, failed antithrombotic therapy, at least 7 days after stroke, and modified Rankin score $\leq$ 3.[6] Exclusion criterion was pregnancy. Stenting and angioplasty were performed in 12 centers in Europe and Asia. Primary end points were "composite ipsilateral stroke/death at 30 days, stent success and procedure success." Follow-up evaluations were at discharge, 30 days and 6 months. Mean age was 66 years. Men comprised 73% of the study population. Of the 45 patients, 42 had stroke as the qualifying event. Eighty percent were taking aspirin and 13% were taking warfarin.

The authors reported: "Among the 45 patients enrolled, the degree of stenosis was reduced from a baseline of 74.9 ± 9.8% to 31.9 ± 13.6% after stenting and 28 ± 23.2% at the 6-month follow-up. The 30-day composite ipsilateral stroke/death rate was 4.5% (2/44). At the 6-month follow-up, the ipsilateral stroke/death rate was 7.0%, the rate for all strokes was 9.7%, and all-cause mortality was 2.3%." Percent restenosis $\geq$ 50% at 6 months was 7.5%. They concluded: "In medically refractory patients with high-grade intracranial atherosclerotic stenoses, a new treatment paradigm involving predilation with an undersized Gateway[™] percutaneous transluminal angioplasty balloon catheter and placement of a self-expanding Wingspan[®] stent system appears to be safe, may facilitate remodeling and may contribute to favorable angiographic outcomes."

In this case series, the sample size was small. There was no control group. Long term outcomes were not available. All patients were placed on clopidogrel for 30 days after stenting and aspirin for life. The number of myocardial infarctions was not reported. The results of this study appear to have been included in the evidence reviewed by the FDA for the Wingspan® HDE approval and summarized in the FDA Summary of Safety and Probable Benefit for the Wingspan® Stent System (available at: http://www.fda.gov/cdrh/pdf5/h050001b.pdf).

Fiorella D, Levy EI, Turk AS, et al. US multicenter experience with the wingspan[®] stent system for the treatment of intracranial atheromatous disease: periprocedural results. Stroke 2007;38:881-887.

Fiorella and colleagues reported the results of the Wingspan® registry (case series) of 78 patients in the U.S. (4 centers) who were treated with the Wingspan® stent system. Of these, 48 (62%) patients presented with strokes. Fifty-nine patients (76%) had a history of antiplatelet therapy failure. Initial percent stenosis was presented in aggregate only, with 54 of 82 (66%) lesions having a 70% stenosis or greater. Stenting and angioplasty were performed in 4 U.S. centers. Mean age was 64 years. Men comprised 58% of the study population.

The authors reported 4 (5.1%) periprocedural deaths and 1 major stroke (1.2%). Postprocedural imaging showed that 34.2% (13/38) of patients had developed new ischemic lesions after the procedure. The authors stated: "At the same time, it is important to note that the periprocedural complications encountered during intracranial PTAS are typically very severe, with 4 of the 5 major complications in the current series resulting in patient death within 30 days." They concluded: "Angioplasty and stenting for symptomatic intracranial atheromatous disease can be performed with the Gateway balloon–Wingspan stent system with a high rate of technical success and acceptable periprocedural morbidity. Our initial experience indicates that this procedure represents a viable treatment option for this patient population."

In this case series, all patients received aspirin and clopidogrel before the procedures and for a minimum of 4 weeks after the procedures. Longer term follow-up (30 days or 6 months) was not reported. The number of myocardial infarctions was not reported. Outcomes were not independently adjudicated.

Layton KF, Hise JH, Thacker IC. Recurrent intracranial stenosis induced by the Wingspan Stent: comparison with balloon angioplasty alone in a single patient. AJNR AM J Neuroradiol 2008; published online.

Layton and colleagues reported the results of a case report of one 68 year old man who underwent angioplasty alone of the left anterior cerebral artery and stent-assisted angioplasty of the left middle cerebral artery. The authors reported: "Follow-up angiography at 4 months documented severe recurrent stenosis confined only to the stented portion of the middle cerebral artery." The patient received aspirin and clopidogrel after the procedure.

Levy EI, Turk AS, Albuquerque FC, et al. Wingspan[®] in-stent restenosis and thrombosis: incidence, clinical presentation and management. Neurosurgery 2007;61:644–651.

Levy and colleagues reported in-stent restenosis (ISR) and thrombosis rates for 78 patients in the Wingspan® registry. ISR was "defined as stenosis greater than 50% within or immediately adjacent (within 5 mm) to the implanted stents and absolute luminal loss greater than 20%." The authors reported: "To date, follow-up imaging (average duration, 5.9 mo; range, 1.5–15.5 mo) is available for 84 lesions treated with the Wingspan[®] stent (78 patients). Follow-up examinations consisted of 65 conventional angiograms, 17 computed tomographic angiograms, and two magnetic resonance angiograms. Of these lesions with follow-up, ISR was documented in 25 and complete thrombosis in four. Two of the 4 patients with stent thrombosis had lengthy lesions requiring more than one stent to bridge the diseased segment. ISR was more frequent (odds ratio, 4.7; 95% confidence intervals, 1.4–15.5) within the anterior circulation (42%) than the posterior circulation (13%). Of the 29 patients with ISR or thrombosis, eight were symptomatic (four with stroke, four with transient ischemic attack) and 15 were retreated. Of the retreatments, four were complicated by clinically silent in-stent dissections, two of which required the placement of a second stent. One was complicated by a postprocedural reperfusion hemorrhage."

The authors concluded: "The ISR rate with the Wingspan[®] stent is higher in our series than previously reported, occurring in 29.7% of patients. ISR was more frequent within the anterior circulation than the posterior circulation. Although typically asymptomatic (76% of patients in our series), ISR can cause neurological symptoms and may require target vessel revascularization." This case series reported findings from the Wingspan® registry, as did the Fiorella study above, and has the same potential methodological issues.

Zaidat OO, Klucznik R, Alexander MJ, et al. The NIH registry on use of the Wingspan stent for symptomatic 70–99% intracranial arterial stenosis. Neurology 2008; published online.

Zaidat and colleagues reported the results of an analysis of the NIH Multi-center Wingspan Intracranial Stent Registry. Sixteen centers enrolled 129 patients with symptomatic 70% to 99% intracranial arterial stenosis who underwent angioplasty and stenting with the Wingspan® stent. The authors reported: "The technical success rate was 96.7%. The mean pre and post-stent stenoses were 82% and 20%. The frequency of any stroke, intracerebral hemorrhage, or death within 30 days or ipsilateral stroke beyond 30 days was 14.0% at 6 months (95% CI = 8.7% to 22.1%). The frequency of 50% restenosis on follow-up angiography was 13/52 (25%)." They concluded: "The use of a Wingspan stent in patients with severe intracranial stenosis is relatively safe with high rate of technical success with moderately high rate of restenosis. Comparison of the event rates in high-risk patients in Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) vs this registry do not rule out either that stenting could be associated with a substantial relative risk reduction (e.g., 50%) or has no advantage compared with medical therapy. A randomized trial comparing stenting with medical therapy is needed."

4. MedCAC

No MedCAC was convened on this issue.

5. Evidence-based guidelines

Not applicable.

6. Professional Societies' Position Statements

Higashida RT et al. Intracranial angioplasty and stenting for cerebral atherosclerosis: A Position Statement of the American Society of Interventional and Therapeutic Neuroradiology (ASITN), Society of Interventional Radiology (SIR), and the American Society of Neuroradiology (AJNR). Am J Neuroradiol 2005;26(9):2323-2327 and J Vasc Interv Radiol 2005;16(10):1281-1285.

In 2005, a multispecialty group published a position statement for the use of intracranial stenting and angioplasty for cerebral atherosclerosis. These societies favor coverage for intracranial angioplasty with or without stenting for intracranial atherosclerotic disease.

- For symptomatic patients with a $\geq$ 50% intracranial stenoses who have failed medical therapy, balloon angioplasty with or without stenting should be considered.
- Patients who have an asymptomatic intracranial arterial stenosis should first be counseled regarding optimizing medical therapy. There is insufficient evidence to make definitive recommendations regarding endovascular therapy in asymptomatic patients with severe intracranial atherosclerosis. They should be counseled regarding the nature and extent of their disease, monitored for new neurological symptoms and have periodic non-invasive imaging at regular intervals of 6-12 months (magnetic resonance angiography or computed tomographic angiography) initially, and then by cerebral angiography if warranted. At a minimum, optimal prophylactic medical therapy should be instituted, which might include antiplatelet and/or statin therapy.
- Continued evaluation and improvements in both pharmacological and catheter-based therapies are needed to reduce the stroke burden from intracranial atherosclerosis.
- Recommend reimbursement by third party insurers so that those patients may have access to such interventions.

The above professional society position statement is the same as we summarized in our previous intracranial stenting and angioplasty decision memorandum and the recommendations have not changed since our last decision.

The Society for Vascular and Interventional Neurology (SVIN), during our second public comment period, provides a position statement (below) with cited references that can be viewed in full on our website at: https://www.cms.hhs.gov/mcd/viewpubliccomments.asp?nca_id=214&rangebegin=02_14_2008&rangeend=03_15_2008

1. "For symptomatic patients with severe (> 70%) intracranial stenosis who have failed best medical therapy (either single anti-platelet therapy such as aspirin or anti-thrombotic therapy such as warfarin), intracranial balloon angioplasty and stenting with devices designed specifically for the cerebral vascular (e.g. Wingspan System) should be strongly considered as a treatment option and should be covered by CMS. Risk factor management for secondary stroke prevention should be encouraged in all patients.

2. For symptomatic patients with severe (> 70%) intracranial stenosis who have failed best medical management (either single anti-platelet therapy such as aspirin or anti-thrombotic therapy such as warfarin), the role of intensive medical therapy (aspirin 325 mg po daily for entire follow-up period and Clopidogrel 75 mg po daily for 90 days plus aggressive risk factor management with blood pressure control <130/80 mm Hg and low-density cholesterol levels of <70 gm/dL) alone or in combination with intracranial balloon angioplasty and stenting needs to be further studied as part of a clinical trial. The SVIN encourages patients who meet the inclusion criteria for the SAMMPRIS trial to be enrolled in this NIH-funded trial.

3. For symptomatic patients with > 50% and < 70% intracranial stenosis who have failed best medical therapy (either single anti-platelet therapy such as aspirin or anti-thrombotic therapy such as warfarin), intracranial balloon angioplasty and stenting with devices designed specifically for the cerebral vasculature (e.g. Wingspan System) should be strongly considered as a treatment option and should be covered by CMS. Risk factor management for secondary stroke prevention should be encouraged in all patients.

4. For symptomatic patients with > 50% intracranial stenosis who have not been on best medical therapy (namely single anti-platelet therapy such as aspirin), there is insufficient evidence currently to make definitive recommendations regarding the role of intracranial balloon angioplasty with or without stenting. Patients should be counseled about the natural history of the disease and the risks of current medical and endovascular therapies. Risk factor management for secondary stroke prevention should be encouraged.

5. For asymptomatic patients with intracranial arterial stenosis, there is insufficient evidence currently to make definitive recommendations regarding the role of intracranial angioplasty with or without stenting. The SVIN encourages researchers to identify high risk groups for stroke among patients with asymptomatic intracranial atherosclerotic disease who might benefit from endovascular therapy. Patients should be counseled about the natural history of the disease and the risks of current medical and endovascular therapies. Best medical therapy including risk factor management for primary stroke prevention should be encouraged.

6. For all patients with intracranial atherosclerotic disease, it should be required by CMS that vascular neurology/neurology consults be obtained prior to treatment with intracranial angioplasty and stenting to ensure that the patient had a stroke or transient ischemic attack and meets the above criteria and is an appropriate candidate for treatment. A vascular neurologist/neurologist should also evaluate the patient following the procedure to objectively assess clinical outcomes to meet CMS quality measures.

7. For all patients with intracranial atherosclerotic disease treated with intracranial balloon angioplasty with or without stenting, hospitals should provide and maintain a local registry in a database accessible by the local IRB as well as CMS, of the intracranial angioplasty and stenting procedural indications, pre-procedure evaluations and post procedural independent neurological assessment of outcomes.

8. To ensure optimal patient outcomes all intracranial balloon angioplasty with or without stenting procedures should be performed by a neuro-interventionalist (Interventional Neurologist, Interventional Neuroradiologist or Endovascular Neurosurgeon) with experience in cerebral micro-catheterization.

9. All intracranial angioplasty with or without stenting procedures should be performed at centers that have extensive experience with these procedures that are also primary or comprehensive stroke centers."

7. Expert Opinion

Comments from Professional Societies and Organizations

CMS received seven public comments during the first public comment period from national professional societies and organizations (AANS and CNS; SIR; ASTIN and SNIS; ASNR; SVIN; SCAI; AAN and ASNR). Four commenters (AANS and CNS; ASITN and SNIS; ASNR; and SVIN) suggested Medicare approve coverage with evidence development (CED) for the use of the Wingspan® stent system. The SIR asks that we reverse the NCD and allow for coverage for intracranial stenting and angioplasty but does not specifically address CED. The SCAI recommends coverage for symptomatic patients with $\geq$ 50% ICAD stenosis or who are not able to take aspirin or who persist with TIA or stroke symptoms after receiving aspirin therapy. The AAN and ASNR support the current Medicare coverage policy of intracranial stenting with angioplasty under an investigational device exemption (IDE) clinical trial and oppose a national coverage decision under CED. The complete proposed decision memorandum and the full summary of all public comments may be located at: http://www.cms.hhs.gov/mcd/viewnca.asp?where=index&nca_id=214&basket=nca:00085R5:214:Intracranial+Stenting+and+Angioplasty:Open:5th+Recon:4

During the second public comment period, we received two public comments from professional societies opposing our proposed decision. The Society for Vascular and Interventional Neurology (SVIN) submitted a position statement, reflected above in Section 6, in addition to their comments (below). The Society for Cardiovascular Angiography and Interventions (SCAI) cites multiple references. The SCAI references can be viewed at: http://www.cms.hhs.gov/mcd/viewpubliccomments.asp?nca_id=214

Comment: The SVIN Professional Society Statement (under section 6, point number three above) recommends that CMS cover intracranial stenting and angioplasty using devices such as the Wingspan® System. In their separate comments, the Society encourages patients to participate in multi-center randomized trials, promotes refinements in "pharmacological and catheter-types treatments" and contends, without CMS allowed coverage, some patients ineligible for the SAMMPRIS trial "will fail to obtain the appropriate" therapeutic approach.

Response: The SVIN comment that "some patients due to ineligibility for the FDA-approved Category B IDE trial will fail to obtain the appropriate therapeutic approach" ignores the feasibility of conducting additional studies that could benefit this population. CMS encourages further research and agrees there is a need for multiple improved approaches that may lead to a better understanding of ICAD and its treatments. CMS concludes that maintaining our existing coverage for intracranial stenting and angioplasty, as stated in this decision memorandum, offers beneficiaries access to this innovative technology, complies with the law and should lead to the progression of knowledge about ICAD and treatments.

Comment: In opposing our proposed decision, the SCAI asks "Why does eligibility for coverage under more than one statute indicate that CMS cannot expand coverage for this procedure?"

Response: With respect to SCAI's general concern about our coverage with evidence development policy, we note that CMS has issued a Guidance Document entitled "National Coverage Determinations with Data Collection as a Condition of Coverage: Coverage with Evidence Development" on July 12, 2006. (http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8). In that document, CMS explained that the Coverage with Study Participation (CSP) form of CED would be used "when the evidence is inadequate to determine that the item or service is reasonable and necessary under section 1862(a)(1)(A)." Page 5. This is in keeping with our principle that "CED will not be used when other forms of coverage are justified by the available evidence." Page 7. We envision that CSP will be used only in rare instances, and do not intend that CED will be used to assume the National Institutes of Health's (NIH's) role in fostering, managing or prioritizing clinical trials. Page 8. Given that we have specifically recognized that coverage for PTA concurrent with Intracranial Stent placement was reasonable and necessary under section 1862(a)(1)(A) when furnished in accordance with the FDA-approved protocols governing Category B IDE clinical trials, additional coverage under CSP is not warranted under our Guidance Document. We also expressly addressed this issue in our proposed decision memorandum at page 13.

The public may submit proposals to revise a guidance document under the procedures established in the Federal Register notice of September 24, 2004 (69 Fed. Reg. 57325). A copy of this notice is available on our website at: http://www.cms.hhs.gov/MedicareCoverageGuideDocs/Downloads/guidance.pdf.

Comment: As an alternative, the Society urges CMS to cover intracranial stenting and angioplasty for two populations. One patient group is composed of those with acute stroke who remain "ineligible" for intravenous thrombolysis but could receive cerebral revascularization. The other patient group includes those with ICAD and $\geq$ 50% stenosis who have had TIA or stroke symptoms and either cannot take aspirin or who persist with symptoms even though aspirin therapy was administered.

The Society notes the lack of "randomized trials" for stenting and angioplasty in patients who are refractory to medical therapy and identifies anomalies such as "chronic occlusions more than 6 months old, long segment occlusions and an occlusion without visible vessels filling distally" that would preclude the use of the intracranial procedure as a desired alternative therapy.

Response: The requestor asks for reconsideration of the NCD for intracranial stenting and angioplasty to allow for Medicare coverage with evidence development for ICAD patients who are medically refractory with $\geq$ 50% intracranial stenosis. The SCAI description of the first sub-population, with acute stroke who remain "ineligible" for intravenous thrombolysis but could receive cerebral revascularization, does not specify the amount of stenosis. If the intracranial stenosis is $\geq$ 50% and the individual participates in an FDA-approved Category B IDE clinical trial, our NCD 20.7.B.5 covers this sub-population. If the stenosis is less than 50% this population falls outside the scope of this NCD and the FDA approval for use of this HDE device. Specifically, based on the CMS evidence review, we believe it is reasonable and necessary to allow "for intracranial angioplasty and stenting of cerebral artery stenosis greater than or equal to 50 percent in patients with intracranial atherosclerotic disease when furnished in accordance with the Food and Drug Administration (FDA)-approved protocols governing Category B Investigational Device Exemption (IDE) clinical trials. All other indications for PTA with or without stenting to treat vertebral or cerebral obstructed lesions remain noncovered." Also, the FDA approved this micro-catheter based delivery system as a HDE used for the treatment of medically refractory ICAD to improve the intracranial vasculature accessible to this device in symptomatic patient with $\geq$ 50% stenosis.

In terms of the second sub-population, those with ICAD and $\geq$ 50% stenosis who have had TIA or stroke symptoms and either cannot take aspirin or who persist with symptoms even though aspirin therapy was administered, they may be covered by the current NCD if they meet the criteria for certain FDA-approved IDE studies as described in our NCD.

We acknowledge our Medicare coverage is restricted and that not all symptomatic TIA or stroke patients with ICAD will meet the eligibility criteria for an IDE study and that these patients may not be interested in participating in an IDE clinical trial. We encourage additional research, support improvements in "pharmacological and catheter-based therapies" as well as continued "approaches to reduce risk factors that may help to prevent TIAs and stroke."

We agree there is a lack of randomized clinical trials for "stenting and angioplasty in patients who are refractory to medical therapy and there are certain conditions that would prohibit the use of the intracranial procedure.

8. Public Comments

A. Initial Public Comment Period

During the initial 30 day public comment period, CMS received fifteen comments and summarized them in our proposed decision that can be viewed on our coverage website at: https://www.cms.hhs.gov/mcd/viewnca.asp?where=index&nca_id=214&basket=nca:00085R5:214:Intracranial+Stenting+and+Angioplasty:Open:5th+Recon:4

To view the public comments submitted via our website please see: http://www.cms.hhs.gov/mcd/viewpubliccomments.asp?id=&cov_id=&state_id=&list_type=&gto=viewpubliccomment&nca_id=214

B. Summary of Comments on the Proposed Decision Memorandum

CMS received 16 comments during this second public comment period including 14 that oppose our proposed decision and two that agree, in part, with the CMS decision. Six comments were modified form letters without new evidence.

With Evidence
(Full disclosure of references can be noted in the public comments section of our website at: http://www.cms.hhs.gov/mcd/viewpubliccomments.asp?nca_id=214&rangebegin=02_14_2008&rangeend=03_15_2008&expand=N)

Comment: The manufacturer does not favor our proposed decision and offers extensive comments. For increased clarity, we separate and identify the comments and responses. First, the requestor reports the Wingspan® System "has been widely accepted by interventional physicians and patient groups" and is a "service covered by many private health insurance plans."

Response: We appreciate the reported stakeholders' acceptance of the Wingspan® System and that health insurance coverage exists for this procedure outside of the Medicare National Coverage Decision. We believe the procedure offers promise and as indicated by our review and analysis allow for restricted coverage and encourage further research.

Comment: A point of agreement between the requestor and CMS is that "coverage of non-IDE trials would provide useful evidence and CMS has covered research studies in similar circumstances under coverage with evidence development (CED)."

Response: We acknowledge this agreement. Although CMS is in favor of additional research, under our CED policy, we will not necessarily seek to fund all research (even studies we would like). We will describe the CED process in more detail in response to a later comment in this section.

Comment: The commenter states "the proposed coverage decision negates the intent of the HDE approval, impeding access to the technology for patients without other therapeutic options and blocks the collection of additional data."

Response: CMS does not have a national HDE policy; however, we have made a national coverage decision for this particular technology at the request of the manufacturer. Based on our review and analysis, we believe our decision provides an avenue for access to the technology and for the collection of additional data related to the HDE population. While we recognize our review and analysis did not result in broad Medicare coverage for this technology, we believe our decision is appropriate based on the existing evidence and facilitates access to this technology. We also acknowledge that there are significant opportunities for expanded studies and that research, outside of an FDA-approved Category B IDE trial, that may be funded by the manufacturer or other community stakeholders to further the shared efforts already made by CMS as demonstrated in our NCD 20.7.5.B, may be warranted.

Comment: While the manufacturer does not dispute the relevance of the CMS cited studies, the requestor was concerned that the CMS analysis included "asymptomatic restenosis measures" and had a decreased emphasis on "stroke and death rate" outcomes. The commenter requests that CMS not use restenosis as a valid measure for determining improved health outcomes. Rather, the commenter urges CMS to recognize "stroke and/or death at various time points as well as changes in the score on a stroke/disability scale" when determining health outcomes related to the intervention. The requestor also asks CMS to consider the "relief of symptoms and threat of stroke" and contends that the risks of stenting are very small compared to the uncertainty faced by medically refractory patients when they do not receive stent intervention.

Response: CMS reviewed new evidence (Levy et al 2007 and Kallmes and Cloft 2008) that was published after our November 2006 consideration and include asymptomatic restenosis measures and discussion that are pertinent to this NCD. Therefore, we did include this information as well as expanded 2008 information (Layton, et al. and Zaidat et al.) in our reconsideration.

We agree it is important to relieve symptoms and to prevent recurrent TIAs and strokes. We look for evidence-based treatments that prove the intervention prevents cerebrovascular and/or death events. We seek sufficient evidence to conclude that there is a cause and effect relationship with findings that are generalizable to the Medicare population and that result in improved health outcomes. We do not anticipate that any one trial will provide all of the answers to the gaps in ICAD knowledge and encourage further research.

Comment: The Company wants Medicare to allow for coverage of the Wingspan® Stent System when performed in an observational study with the rationale for doing so cited below.

- "Results from an observational study will add to the SAMMPRIS trial data and could serve as evidence for other coverage decisions and for use by physicians to enhance the management of ICAD.
- Medicare coverage would improve access to this technology for a small group of beneficiaries who are medically refractory to drug therapy."

Eight other commenters, including 6 modified form letters, endorsed observational studies as outlined by the requestor.

One commenter, based on the WASID trial, opposes our proposed decision and asks CMS to "support studies and data collection to confirm the efficacy of intracranial stenting in the cohort of patients not covered by the SAMMPRIS trial."

Response: While CMS generally supports the need for more research, the CED Guidance document explains that the use of CSP is intended to be rare and Medicare has not declared an intent to finance all worthwhile research under §1862(a)(1)(E). Instead, CMS' funding of research remains at our discretion. We do not know that intracranial stenting and angioplasty will prevent recurrent stroke, TIA or death and believe that there are abundant opportunities for expanded research that may be funded by the manufacturer or other stakeholders.

Comment: The requestor reports that there are existing NCDs that involve CED that have varying decisions that illustrates that our proposed decision memo for the Wingspan® System is inconsistent with other CED decisions. The commenter also finds it troublesome that the statutes described in our proposed decision memorandum lack "mutual exclusivity" in these other decisions which is different from the position we have reached in the Wingspan® System decision.

Response: Each NCD request is unique based on the evidence in the record. Each NCD receives a full CMS review and analysis. We practice transparency in this process and maintain website postings for each of these decisions. In our view, the intracranial stenting and angioplasty reconsideration is the first time CMS has considered the Coverage with Study Participation (CSP) form of CED for a population that was already covered under §1862(a)(1)(A).

Our policies related to Coverage with Evidence Development are set forth in our Guidance Document available at http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8. We have never intended to use CSP to help finance all potential medical research.

-

- With respect to Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnea (OSA) (CPAP) (CAG-00093R2), CSP is being offered for a population that would not be covered under §1862(a)(1)(A).

- In terms of the Artificial Heart decision (CAG-00322N) there was previously a national non-coverage determination so no distinct populations were previously covered.

We have applied the final guidance policy consistently.

Comment: The manufacturer speculates that the FDA would not approve an IDE trial for this population for the purpose of "collecting safety and effectiveness data" and that the FDA "would not issue an IDE for a study of only on-label HDE patients" as "individuals with 50-69% stenosis who have not had a stroke should first be managed on medical therapy."

Response: CMS is not in a position to evaluate the manufacturer's speculation that FDA would not approve an IDE trial for this population. CMS recommends that the manufacturer consult with FDA directly about the possibility of obtaining an approved IDE under 21 CFR Part 812. See http://www.fda.gov/CDRH/DEVADVICE/ide/applications.html.

Comments: The Company opines that a CED barrier doesn't exist because the current intracranial stenting and angioplasty coverage is restricted; therefore, additional coverage, under section 1862(a)(1)(E), is not only feasible but does not include "statutory language" that would limit "coverage to a single authority." Additionally, the manufacturer proposes that "medically refractory patients with intracranial artery stenosis > 50% but < 70% would not be covered under section 1862(a)(1)(A) coverage because they are not eligible for the [existing] IDE study."

Response: Our previous analysis found adequate evidence to expand coverage to allow for intracranial stenting and angioplasty in FDA-approved Category B IDE clinical trials for patients with cerebral artery stenosis $\geq$ 50%. Under our CED policy, CSP can only be used in circumstances where no Medicare coverage for a particular population is available under §1862(a)(1)(A).

Comment: The writer states that CMS did not "establish and follow clear standards consistent with the Medicare statute governing the coverage decision-making process;" and that there is no "clear guidance on how the standards for coverage are applied and no discernible patterns for decisions." The requestor disputes how CMS applies a standard for "adequate evidence" in this NCD. Specifically, when there is "sufficient evidence to merit coverage under section 1862(a)(1)(A)" the requestor concurrently believes "that same evidence that CMS relied on to allow coverage conditioned on patients being in an IDE trial also could be relied on to allow coverage conditioned on patients being in a study that involves IRB approval consistent with 21 [Code of Federal Regulations] C.F.R. Part 56 and requires informed consent consistent with 21 C.F.R. Part 50." The requestor asks for "a full written explanation of its policy and legal rationales for not extending coverage under this request."

Response: We recognize that the manufacturer of the device is disappointed with our proposed decision that would retain our existing coverage, and does not expand coverage for patients in additional studies as requested. We have attempted to explain our reasoning, as guided by our published Guidance Document. Perhaps no explanation would be deemed satisfactory given the company's unique perspective. Still, when making this NCD, like all NCDs, CMS followed an open and transparent process. See 68 Fed. Reg. 55,634 (Sept. 26, 2003). There were two opportunities for public participation, and we have responded to the public comments as required by §1862(1) of the Social Security Act. Several commenters, including a medical specialty society without a direct financial stake in the outcome, understood and agreed with our analysis of the evidence. We note that the Medicare statute and our regulations provide opportunities for certain aggrieved parties to challenge our NCDs. See §1869(f); 42 C.F.R. Part 426. For transparency in our NCD process, the final decision memorandum is the mechanism that has been established and we will use that method and vehicle to address all concerns and opinions to complete this NCD process.

Without Evidence
Comment: A national health association writes their concurrence, in part, with our proposed decision. This association contends that there is the potential for biases when there are no control groups or failure to provide long term follow-up in the case series data submitted for our review and analysis; and, therefore, there is "inadequate evidence" to determine the clinical benefit related to this procedure to allow for Medicare coverage in settings other than clinical trials. In their expressed understanding of the statutory limitation that will not permit CMS to expand coverage for this system, they offer the following two parameters for CMS to consider for CED.

1. "This procedure shows promise for the treatment of a serious condition with significant risk of associated morbidity and mortality and for which there are few or no effective therapies currently available.
2. Patient recruitment for clinical trials has been slow given the small number of patients with this condition and the relatively small number of sites where the procedure is performed. Without CED, therefore, it will be a difficult and lengthy process before there are adequate data on patient outcomes to be able to evaluate the procedure's safety and effectiveness."

Response: CMS agrees there is limited peer-reviewed literature and that there may be few eligible or willing participants for clinical trials to accommodate the rapid development of additional data. However, in contrast to this group's comment, we conclude there is "adequate" evidence for restricted Medicare coverage of the Wingspan® System as evidenced by our NCD 20.7.B.5.

Comment: A stakeholder agrees, in part, with CMS and states there is not enough evidence to prove intracranial stenting and angioplasty will decrease stroke risk in the defined population and suggests, beyond what CMS has proposed in our decision memorandum that CMS pay for this system when patients are selectively enrolled in "trials or registries."

Response: CMS appreciates the agreement that there is a need for additional research, supports the community in the expansion of studies and covers selected patient participation in restricted trials as outlined in our November 6, 2006 decision memorandum and our CED Guidelines.

Comment: A community association wants increased beneficiary access to new medical technologies and opposes the CMS proposed decision. To further access, this group would like CMS to allow beneficiaries access to HDE treatments through the CED process and when non-coverage decisions occur, recommends a quick completion of the NCD process. In circumstances where no national coverage determination exists, the association maintains support for contractor discretion when making HDE determinations.

Response: National coverage decisions that expand beneficiary access to new medical technologies are based on a critical review and analysis of existing evidence and take into consideration the risks and benefits involved in implementing such technologies. CMS does not have an HDE policy but conducts a specific NCD review when appropriately requested. In the absence of a national coverage determination, we defer to the local contractors to determine coverage for HDEs.

Comments: The other concern for this writer relates to our statutory basis for denying "coverage with study participation under CED" for intracranial stenting and angioplasty. Specifically, the commenter states "eligibility for coverage in an IDE clinical study should not prevent a technology from being eligible for CED. CMS can, and does, employ various approaches to coverage that involve evidence generation." They contend that these two pathways, statutes: §1862(a)(1)(A) and §1862(a)(1)(E), can and should be combined and used simultaneously to allow for the evolution of evidence for this technology that is the only reasonable alternative treatment for this population. In addition, several commenters express difficulty understanding the differences between Sections 1862(a)(1)(A) and 1862(a)(1)(E) of the Social Security Act and how these statutes are applied to our decision. One commenter writes that the law is without merit and outdated.

Response: As noted earlier, our policies related to Coverage with Evidence Development are set forth in our Guidance Document available at http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8. We have never intended to use CSP to help finance all potential medical research. With respect to the comment that the Medicare Act is outdated, this concern is outside the purview of a national coverage determination.

Comment: A physician's assistant opposes the CMS proposed decision and opines that Medicare should reimburse for endovascular therapy that [reportedly] prevents "symptomatic" patients from experiencing further "symptoms" or from experiencing "an ischemic cerebrovascular" event. The commenter concludes that for Medicare to pay for stroke-related-care and not to reimburse for a "proven technology and procedures that reduce the risk of stroke" does not make sense.

Response: There is a great deal we do not know about this disease and procedure and in particular about the data concerning long term stroke prevention and endovascular therapy. Currently, the two trials that involve endovascular therapy for intracranial atherosclerosis are: 1) the Stenting of Symptomatic Atherosclerotic Lesions in the Vertebral or Intracranial Arteries (SSYLVIA); and 2) the Wingspan Trials (SSYLVIA Study). The findings in these trials do not include long term stroke prevention data**.** Another major gap in our knowledge and of concern to CMS is whether the findings in the research can be generalized to the Medicare population. Consequently**,** in addition to Medicare's current coverage of FDA-approved Category B IDE studies, there are numerous opportunities for further research; and we strongly encourage the involvement of additional stakeholders, in this broad research endeavor, to assume some responsibility for increasing beneficiary access to this technology that may contribute to increased knowledge about the disease and the procedure.

Comment: A commenter reveals patients do not want to go into debt to pay for this stenting but instead elect not to have the procedure. Also**,** from a reimbursement perspective**,** six other commenters submit form-type letters that state the CMS proposed decision adversely and "directly affects" their "hospital's financial ability to provide this endovascular treatment to these patients."

Responses: CMS does not consider costs when making national coverage decisions. However, as mentioned above, there are numerous opportunities for multiple stakeholders to share in the responsibility for advancing the science and clinical applications related to this disease and technology.

Comments: Many commenters point to the population differences between those in the SAMMPRIS trial versus those in the observational study.

Response: CMS recognizes the differences between the SAMMPRIS trial and the Boston Scientific proposed observational study. We solicit new and relevant evidence and eagerly await the findings from future relevant research. The SAMMPRIS randomized trial is designed to determine health outcomes comparing optimal medical therapy to stenting and includes a 2 year mean follow-up; whereas the observational study may provide additional device safety and efficacy data but will be limited in its ability to prove cause and effect relationships.

Comment: An association expresses concern about the "implications resulting from CAG00085R5 for coverage for humanitarian use devices;" and "the impact on the application of coverage with evidence development." This group states "Medicare beneficiaries should have covered access to medical technologies that have received a humanitarian device exemption from the Food and Drug (FDA)"and reports "CMS can facilitate beneficiary access to HDEs by making the CED process an intermittent conduit for coverage for those HDEs subject to national non-coverage determinations." This commenter also contends "in the absence of a national coverage decision, CMS should allow local contractor judgment in determining the appropriateness of HDE coverage." To address [alleged] inconsistencies in how the statutes have been interpreted by CMS, the group provides the following.

"CMS maintains the authority to use different approaches to cover a device requiring further development of evidence. However, a device should not become ineligible for coverage under CED due to the fact that the device may be qualified for coverage under an IDE clinical study. CMS maintains the authority to employ a CED approach under §1862(a)(1)(E) if additional evidence is needed to determine whether a given technology or service is "reasonable and necessary. CMS further maintains authority to provide coverage to a technology if it is being studied in a Category B IDE clinical study pursuant to §1862(a)(1)(A). Using both approaches to coverage will allow for greater development of evidence that CMS is increasingly requiring."

Response: In this NCD reconsideration request, the manufacturer did not indicate a different population, so this review has focused on the same population as the prior analysis. The 2006 CMS decision found adequate evidence to support "reasonable and necessary" for restricted Medicare coverage of the Wingspan® Stent System when applied to a specified population under §1862(a)(1)(A). Furthermore, as described in our Analysis (Section VIII below), "our Guidance Document on Coverage with Evidence Development, the Coverage with Study Participation (CSP) form of CED is applicable only for items and services where the medical evidence is not adequate for coverage under section 1862(a)(1)(A)."

To the extent that changes in the CED policy are desired, the public may submit proposals to revise a guidance document under the procedures established in the Federal Register notice of September 24, 2004 (69 Fed. Reg. 57325). A copy of this notice is available on our website at http://www.cms.hhs.gov/MedicareCoverage GuideDocs/Downloads/guidance.pdf.

To conclude the public comments section, we note that Medicare continues to cover PTA and stenting of intracranial arteries for the treatment of cerebral artery stenosis $\geq$ 50% in patients with intracranial atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE trials.

VIII. CMS Analysis

National coverage determinations are determinations by the Secretary with respect to whether or not a particular item or service is covered nationally under title XVIII of the Social Security Act §1869(f)(1)(B). In order to be covered by Medicare, an item or service must fall within one or more benefit categories contained within Part A or Part B, and must not be otherwise excluded from coverage. Moreover, with limited exceptions, the expenses incurred for items or services must be "reasonable and necessary for the diagnosis or treatment of an illness or injury or to improve the functioning of a malformed body member," §1862(a)(1)(A).

We previously found that PTA and stenting of intracranial arteries for the treatment of cerebral artery stenosis ≥ 50% in patients with intracranial atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE clinical trials was reasonable and necessary under §1862(a)(1)(A).

The previous CMS decision was restricted to PTA and stenting and this reconsideration request includes angioplasty with stenting; therefore, we are not addressing PTA without stenting in this proposed decision.

Our analysis focused on the following question:

- Is the evidence sufficient to conclude that percutaneous transluminal angioplasty and stenting of symptomatic intracranial artery stenosis ≥ 50% improves health outcomes?

Since our prior decision on intracranial PTA and stenting in November 2006, 5 studies (Bose, Fiorella, Levy, Layton, Zaidat) have been published that presented data using the Wingspan® stent system. The study by Bose presented data that appears to have been the basis for the FDA decision and summary of safety and probable benefit (see: http://www.fda.gov/cdrh/pdf5/h050001b.pdf). Although the data were not published at the time, this evidence was considered in our November 2006 decision and is not considered new evidence for this reconsideration.

The Fiorella and Levy studies presented data from the Wingspan® registry of 78 patients. Zaidat and colleagues reported on the NIH Wingspan registry of 129 patients. These studies, as with all case series type studies, are difficult to interpret without additional studies that reduce the possibility of inherent biases and substantiate the clinical findings. Various biases may have been factors in the observed differences in the registry data compared to the initial Wingspan® study presented by Bose. Levy and colleagues reported: "The ISR (in-stent restenosis) rate with the Wingspan[®] stent is higher in our series than previously reported, occurring in 29.7% of patients." In addition, the lack of control groups and long term follow-up add to the uncertainty of clinical benefit. We are concerned that Levy et al. considers in-stent dissections to be "clinically silent," particularly in view of their treatment with a second stent. Concerns were also noted by Kallmes and Cloft (Kallmes 2008) who reported: "The overall restenosis rate in the study by Levy et al. was 31%, even though they excluded 4 cases of complete occlusion. Including those cases of complete occlusion would have increased the reported rate of restenosis by approximately 4%." A higher restenosis rate (25%) and adverse outcome rate (14%) were also seen in the analysis by Zaidat and colleagues, although the patients enrolled in the NIH registry had greater stenosis (70-99%) compared to the other registry.

Given the invasive nature of this treatment and the severe risks, as noted by Fiorella and colleagues, a well designed, well conducted randomized controlled trial is needed. The need for a randomized controlled trial was noted by Derdeyn and Chimowitz (2007) who stated: "At present, however, there is no level 1 evidence to support angioplasty and stenting for patients who have symptomatic intracranial atherosclerotic disease. Case series suggest that the safety and stroke risk reduction of this procedure may provide a benefit, particularly with self-expanding stent technology. A randomized, controlled trial is needed to prove the efficacy of this therapy." Kallmes and Cloft wrote: "We, the community of physicians, really have to continue to ponder what the real value of Wingspan[®] is, and we must demand more data about safety and efficacy relative to other treatment options."

CMS believes the evidence is promising and strongly encourages the development and completion of randomized controlled trials and currently covers PTA and stenting for the treatment of intracranial artery stenosis greater than or equal to 50 percent in patients with atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE clinical trials. There is a newly funded clinical trial titled "Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS)" designed to determine health outcomes comparing optimal medical therapy to stenting and includes a 2 year mean follow-up. This randomized trial is expected to provide solid evidence on this intervention. Additional non-IDE trials would provide useful evidence as well and, in previous NCDs, we have covered research studies under the concept "Coverage with Evidence Development (CED)." However, as outlined in our Guidance Document on Coverage with Evidence Development, the Coverage with Study Participation (CSP) form of CED is applicable only for items and services where the medical evidence is not adequate for coverage under section 1862(a)(1)(A). CMS has never intended to use CSP to financially support all medical research that may be significant for the Medicare population. Indeed we have noted that the CSP form of CED is to be used rarely and do not intend to assume the role of other agencies that finance medical research. In our existing NCD, 20.7.B.5, coverage exists under §1862(a)(1)(A) for beneficiaries in certain IDE trials, preventing any further expansion for these individuals under section 1862(a)(1)(E). Therefore, coverage continues to be available to specified Medicare beneficiaries in certain IDE trials under the NCD. To further clarify based on these findings, CMS is not extending coverage to hospitals that are not conducting FDA-approved Category B IDE clinical trials and any use of intracranial stenting outside an IDE clinical trial would be non-covered.

IX. Summary

We have fully considered Boston Scientific Corporation's request to reconsider our National Coverage Determination (NCD) on percutaneous transluminal angioplasty (PTA) with intracranial stent placement that is published at 20.7.B.5 of the Medicare National Coverage Determinations Manual. After considering additional evidence and information, including the timely public comments as required by §1862(1) of the Social Security Act, we are reaffirming our existing national coverage decision and will not expand coverage as requested. Medicare will continue to cover PTA and stenting of intracranial arteries for the treatment of cerebral artery stenosis $\geq$ 50% in patients with intracranial atherosclerotic disease when furnished in accordance with the FDA-approved protocols governing Category B IDE trials. CMS will continue our national non-coverage for all other indications for PTA with or without stenting to treat obstructive lesions of the vertebral and cerebral arteries.

APPENDIX A

General Methodological Principles of Study Design
(Section VI of the Decision Memorandum)

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service is reasonable and necessary. The overall objective for the critical appraisal of the evidence is to determine to what degree we are confident that: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients.

We divide the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the generalizability of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's potential risks and benefits.

The methodological principles described below represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has its unique methodological aspects.

Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias).
- Co-interventions or provision of care apart from the intervention under evaluation (performance bias).
- Differential assessment of outcome (detection bias).
- Occurrence and reporting of patients who do not complete the study (attrition bias).

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, in general, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The design, conduct and analysis of trials are important factors as well. For example, a well designed and conducted observational study with a large sample size may provide stronger evidence than a poorly designed and conducted randomized controlled trial with a small sample size. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess and consider the evidence.

Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage determinations for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation) and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations. One of the goals of our determination process is to assess health outcomes. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived. Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

---

[1] Decision Memo for Intracranial Stenting and Angioplasty (CAG-00085R2) http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=177

[2] http://www.cms.hhs.gov/manuals/downloads/ncd103c1_Part1.pdf

[3] http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfHDE/HDEInformation.cfm [This website has not been updated since passage of FDAAA, which amended the HDE provision.]

[4] http://www.fda.gov/cdrh/pdf5/h050001a.pdf

[5] http://www.fda.gov/cdrh/ode/hdeinfo.html [This website has not been updated since passage of FDAAA, which amended the HDE provision.]

[6] The modified Rankin score provides criteria for patient selection, as noted below (Wilson, 2002):

Modified Rankin Stroke Scale
0 – No symptoms at all.
1 – No significant disability despite symptoms; able to carry out all usual duties and activities.
2 – Slight disability; unable to carry out all previous activities but able to look after own affairs without assistance.
3 – Moderate disability; requiring some help, but able to walk without assistance.
4 – Moderately severe disability: unable to walk without assistance and unable to attend to own bodily needs without assistance.
5 – Severe disability: bedridden, incontinent and requiring constant nursing care and attention.

Back to Top

Bibliography

Bose A, Hartmann M, Henkes H, et al. A novel, self-expanding, nitinol stent in medically refractory intracranial atherosclerotic stenoses: the Wingspan study. Stroke 2007;38:1531-1537.

Chimowitz MI, Kokkinos J, Strong J, Brown MB, Levine SR, Sillman S, et al. The warafarin-aspirin symptomatic intracranial disease study. Neurology 1995;45:1488-1493.

Chimowitz MI, Lynn MJ, Howlett-Smith H, Stern BJ, Hertzberg VS, Frankel MR, et al. Comparison of warfarin and aspirin for symptomatic intracranial arterial stenosis. N Engl J Med 2005;352:1305-1316.

Derdeyn CP, Chimowitz MI. Angioplasty and stenting for atherosclerotic intracranial stenosis: rationale for a randomized clinical trial. Neuroimag Clin N Am 2007;17:355–363.

Fiorella D, Levy EI, Turk AS, et al. US multicenter experience with the wingspan stent system for the treatment of intracranial atheromatous disease: periprocedural results. Stroke 2007;38:881-887.

Food and Drug Administration. Humanitarian Use Devices.2003 (available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/HDEInformation.cfm).

Food and Drug Administration. Wingspan Stent System with Gateway PTA Balloon H050001. Approval Order. 2005 (available at: http://www.fda.gov/cdrh/pdf5/h050001a.pdf)

Food and Drug Administration. Wingspan™ Stent System with Gateway™ PTA Balloon Catheter: Summary of safety and probable benefit. (Available at: http://www.fda.gov/cdrh/pdf5/h050001b.pdf).

Henkes H, Miloslavski E, Lowens S, et al. Treatment of intracranial atherosclerotic stenoses with balloon dilatation and self-expanding stent deployment (WingSpan). Neuroradiology 2005;47:222-228.

Higashida RT, et al. Intracranial angioplasty and stenting for cerebral atherosclerosis: A position Statement of the American Society of Interventional and Therapeutic Neuroradiology, Society of Interventional Radiology and the American Society of Neuroradiology. Am J Neuroradiol 2005;26(9):2323-2327 and J Vasc Interv Radiol 2005;16(10):1281-1285.

Kallmes DF, Cloft HJ. How do we spin Wingspan? Am J Neuroradiol 2008;29:28-29.

Kasner, SE, Chimowitz MI, Lynn MJ, et al. Predictors of ischemic stroke in the territory of a symptomatic intracranial arterial stenosis, American Heart Association. Circulation 2006; 113:555-563.

Kasner, SE, Lynn MJ, Chimowitz MI, et al. Warfarin vs. aspirin for symptomatic intracranial stenosis: Subgroup analyses from WASID. Neurology 2006;67:1275-1278.

Layton,KF, Hise JH, Thacker IC. Recurrent intracranial stenosis induced by the Wingspan Stent: comparison with balloon angioplasty alone in a single patient. AJNR Am J Neuroradiol 2008; Available at: http://www.ncbi.nlm.nih.gov/pubmed/18372421?ordinalpos=1&itool=EnrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVMedline.

Levy EI, Turk AS, Albuquerque FC, et al. Wingspan in-stent restenosis and thrombosis: incidence, clinical presentation and management. Neurosurgery 2007;61:644–651.

Marks MP, Marcellus ML, Norbash AM, et al. Outcome of angioplasty for atherosclerotic intracranial stenosis. Stroke 1999;30:1065-1069.

Marks MP, Marcellus ML, Do HM, et al. Intracranial angioplasty without stenting for symptomatic atherosclerotic stenosis: Long-term follow-up. ANJR 2000;26:525-530.

Marks, MP, Wojak JC, Al-Ali F, et al. Angioplasty for symptomatic intracranial stenosis: clinical outcome. Stroke 2006;37:1016-1020.

Medicare National Coverage Determination (NCD) Manual, NCD for Artificial Heart. See: http://www.cms.hhs.gov/mcd/viewnca.asp?where=index&nca_id=211&basket=nca:00322N:211:Artificial+Hearts:Closed:New:10 .

Medicare National Coverage Determination (NCD) Manual, NCD for Continuous Positive Airway Pressure (CPAP) Therapy for Obstructive Sleep Apnea (OSA) (CPAP). See: http://www.cms.hhs.gov/mcd/viewnca.asp?where=index&nca_id=204&basket=nca:00093R2:204:Continuous+Positive+Airway+Pressure+%28CPAP%29+Therapy+for+Obstructive+Sleep+Apnea+%28OSA%29:Closed:2nd+Recon:14.

Medicare National Coverage Determination (NCD) Manual, National coverage determination with data collection as a condition of coverage: coverage with evidence development. See: http://www.cms.hhs.gov/mcd/ncpc_view_document.asp?id=8.

Medicare National Coverage Determination (NCD) Manual, NCD for percutaneous transluminal angioplasty (PTA) (20.7). Available at: http://www.cms.hhs.gov/mcd/viewncd.asp?ncd_id=20.7&ncd_version=4&basket=ncd%253A20%252E7%253A4%253%20A%20Percutaneous+Transluminal+Angioplasty+%2528PTA%2529.

The Centers for Medicare and Medicaid Services. Decision memo for intracranial stenting and angioplasty (CAG-00085R2). Available at: http://www.cms.hhs.gov/mcd/viewdecisionmemo.asp?id=177.

Thijs VN, Albers GW. Symptomatic intracranial atherosclerosis. Outcome of patients who fail antithrombotic therapy. Neurology 2000;55:490-497.

Wilson JT, Hareendran A, Grant M, et al. Improving the assessment of outcomes in stroke: use of a structured interview to assign grades on the modified Rankin scale. Stroke 2002;33:2243-2246.

Zaidat OO, Klucznik R, Alexander MJ, et al. The NIH registry on use of the Wingspan stent for symptomatic 70-99% intracranial arterial stenosis. Neurology 2008; Available at:http://www.ncbi.nlm.nih.gov/pubmed/18235078?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum.

Back to Top